1182-68 Failing of Left Ventricular β Adrenergic Affinity in a Canine Model of Obesity-Hypertension

P. Cabrol, M. Galinier, J. Fourcade, P. Léger, J.L. Montastruc, J.P. Bounhoure, J.M. Fauvel, J.M. Sénard. *University of Toulouse, France*

Background: Obesity constitues a classic supplier of cardiovascular diseases. This work assess cardiac β adrenergic phenotype in obesity hypertension before heart failure appears.

Methods: Six beagle dogs (aged 35 ± 5 months) receiving during 30 weeks a high-fat diet were compared to 6 normal beagle dogs. Cardiac β adrenergic receptor density were mensured by a binding study with iodocyanopindolol. β1 and β2 densities were obtained by competition with CGP 20712A. Affinity state of β adrenergic receptor was assessed by competition with isoproterenol. Noradrenaline plasma level was assayed by HPLC. Left ventricular mass were measured by echocardiography.

Results: Systolic blood pressure was higher in obeses (245 ± 8 vs 197 ± 10 mmHg in controls). Diastolic blood pressure didn't differed between both group (93 ± 3 vs 84 ± 3 mmHg in controls). Noradrenaline plasma levels were not differents between the both groups (276 ± 30 vs 235 ± 50 pg/ml in controls). Obeses were characterized by higher left ventricular mass (80 ± 24 vs 67 ± 15 g in controls). β-AR right auricular and left ventricular density were not respectively different in obeses (57 ± 6 and 67 ± 4 femtoM/mg protein) compared to controls (68 ± 7 and 63 ± 9 femtoM/mg protein). β1-AR proportion were the same between obeses and controls in right auricular (63 ± 4 vs 64 ± 3% in controls) and left ventricular (59 ± 3 vs 60 ± 4% in controls). Proportion of β-AR receptors in a high affinity state were the same in auricular sample (69 ± 4 vs 67 ± 3% in controls) but was different in left ventricular (28 ± 6 vs 74 ± 6% in controls)

Conclusion: Left ventricular β-adrenoceptor came under a specific desensibilisation in this obesity-hypertension model independent of plasma noradrenaline levels. This changes may account to the progressive systolic dysfunction.

1182-69 Decreased Urinary Excretion of Urodilatin in Patients With Essential Hypertension

Y.-S. Hwang, Y.-J. Lee, J.-D. Wen, S.-J. Shin, J.-H. Tsai. *Kaohsiung Medical College, Taiwan*

Background: Urodilatin is a renal synthesized peptide with potent natriuretic activity and is thought to play a role in the renal handling of sodium homeostasis. This study is designed to investigate the possible role of urodilatin in the pathogenesis of essential hypertension (EH).

Methods: Urinary atrial natriuretic peptide-like immunoreactivity (ANP-LI) excretion was measured by radioimmunoassay (RIA) after extraction in twenty-three EH patients without any detectable target organ damage and eleven normotensive control subjects. High performance liquid chromatography (HPLC) coupled with RIA was used to characterize the molecular natures of ANP-LI in the urine. Urinary concentrations of urodilatin were measured by a competitive ELISA with urodilatin specific antibody.

Results: Urinary excretion of ANP-LI in patients with EH (13.7 ± 1.8 ng/day) was not significantly different from that of control subjects (14.4 ± 2.4 ng/day). The HPLC couples with RIA revealed that the major components of ANP-LI in the urine are α-hANP and urodilatin. The molar ratio of α-hANP: urodilatin in the urine was 40.9: 59.1 in normal subjects, while the urodilatin molar ratio is significantly decreased in patients with EH (71.3: 28.7).

Conclusion: The decreased urodilatin excretion in patients with EH may suggest that urodilatin is involved in the pathogenesis of EH.

1182-70 Transforming Growth Factor β2 Levels in Patients With Essential Hypertension – The Effect of Antihypertensive Treatment With Ramipril

Th.K. Makris, P.G. Krespi, A.N. Hatzizacharias, V.E. Votteas, E.B. Chronakis, C.G. Tsoukala, N.G. Stratigis, M.K. Kyriakidis. *Cardiology Dept. 2nd Reg. BTC-Haemost. Lab., Laikon Gen. Hosp., Athens, Greece*

Background: Transforming Growth Factor (TGF) acts either as an inhibitor or as stimulant of proliferation and differentiation or by modulating cell functions. It has been also implicated with a variety of other locally synthesized factors in dramatic structural disorders in pathologies such as atherosclerosis and hypertension. The aim of our study was: a) to determine $TGF_{\beta 2}$ levels in hypertensive patients (pts) and b) to examine the effect of antihypertensive treatment (i.e. ramipril) on the $TGF_{\beta 2}$ levels in the same population.

Methods: 43 hypertensives (20 M, 23 F) mean age 52.2 ± 10.6 yrs with mild to moderate arterial hypertension (DBP 100 ± 9 mmHg, Group H) and 40 healthy volunteers (19 M, 21 F) mean age 48.7 ± 10.3 yrs (Group N) were studied. Blood sampling was performed at 8–9 am after 12 hours of fasting. $TGF_{\beta 2}$ levels were assayed by ELISA. In the hypertensive group measurements were made before (baseline) and six months after therapy with ramipril.

Results: The $TGF_{\beta 2}$ plasma levels were significantly higher in the hypertensive group (38.9 ± 5.3 pg/ml) than in healthy volunteers (36.25 ± 3.99 pg/ml) $p < 0.05$. Antihypertensive therapy with ramipril had a favorable effect, i.e. significant decrease of the $TGF_{\beta 2}$ levels in the hypertensive group (35.72 ± 4.68 vs 38.9 ± 5.3 pg/ml, $p < 0.01$).

Conclusion: Our findings suggest that $TGF_{\beta 2}$ levels are significantly increased in hypertensives compared to healthy volunteers ($p < 0.05$). Moreover, antihypertensive therapy with ramipril affects these levels favorably. These observations raise the possibility that $TGF_{\beta 2}$ may be another marker of the effectiveness of antihypertensive therapy.

1183 Treatment of Cardiovascular Disease in the Elderly

Wednesday, April 1, 1998, 9:00 a.m.–11:00 a.m.
Georgia World Congress Center, West Exhibit Hall Level
Presentation Hour: 10:00 a.m.–11:00 a.m.

1183-71 Suppression of Sympathetic Nervous System Activity and Increased Inotropic β-Receptor Responsivity During Metoprolol Therapy in Elderly Patients With CHF

M.A. Supiano, M.R. Starling. *Department of Internal Medicine, Cardiology and Geriatrics Sections, University of Michigan; VA Medical Centers, Ann Arbor, MI, USA*

Aging and CHF are each associated with sympathetic nervous system activation (SNSa) and decreased β-receptor responsiveness. To determine if chronic β-blocker therapy would result in suppression of SNS activity and up-regulation of β-receptor responsivity in older CHF patients, we measured plasma norepinephrine (NE) levels, ^{3}H-NE kinetic parameters, and inotropic (dobutamine-mediated increase in velocity of circumferential fiber shortening, ΔVCF_c) β-receptor response in 7 subjects aged 62–79 yrs with LV systolic dysfunction (ejection fraction <40%) at baseline and following 6 months of metoprolol therapy. Compartmental analysis of plasma NE and ^{3}H-NE levels obtained during ^{3}H-NE infusion and during its decay was performed to determine the extravascular NE release rate (NE_2), an index of systemic SNSa, and NE metabolic clearance rate (MCR_1).

	NE (pg/ml)	NE_2 (μg/min/m²)	MCR_1 (l/min/m²)	VCF_c (circ/sec)	ΔVCF_c (circ/sec)
Baseline	393 ± 26	2.23 ± 0.15	1.17 ± 0.08	0.89 ± 0.05	0.16 ± 0.04
Metoprolol	304 ± 33	1.84 ± 0.17	1.02 ± 0.08	1.04 ± 0.10	0.27 ± 0.05
P value	0.01	0.004	0.06	0.17	0.05

Following metoprolol: 1) despite a fall in MCR_1, plasma NE levels were significantly lower due to a decrease in NE_2, suggesting suppression of SNSa; and 2) VCF_c tended to increase, and the ΔVCF_c was significantly improved, suggesting enhanced myocardial contractility and an up-regulation of inotropic β-receptor responsivity. There was also a significant improvement in 6-min walk distance (1268 ± 29 to 1370 ± 41 ft; P = 0.02). Thus, chronic β-blocker therapy in older patients with CHF appears to suppress SNSa, improve inotropic β-receptor responsivity, and is associated with improved functional performance.

1183-72 Plasma Atrial and Brain Natriuretic Peptides in Elderly Patients With Heart Failure due to Diastolic vs. Systolic Left Ventricular Dysfunction

C.T. Marburger, P.H. Brubaker, T.M. Morgan, B. Brosnihan, D.W. Kitzman. *Bowman Gray School of Medicine of Wake Forest University, Winston-Salem, North Carolina, USA*

We recently reported that elderly patients with heart failure and a normal LV ejection fraction (EF 69 ± 9%) and no coronary, valvular, or pulmonary disease (presumed diastolic dysfunction, DD) have severe exercise intolerance equal to age-matched patients with severe systolic LV dysfunction (SD, EF 29 ± 10%). We now report plasma concentrations of atrial (ANP) and brain (BNP) natriuretic peptides by radioimmunoassay (CV 6% and 11% respectively) in these patients and in healthy age-matched volunteers (HV) during supine rest (REST), head up tilt table (TILT) and maximal bicycle exercise (EXER). Data shown as mean ± SEE. *$p < 0.05$ and **$p < 0.01$ vs HV) after log transformation and adjustment for age and gender.

	n	ANP			BNP		
		rest	tilt	exer	rest	tilt	
HV	21	14 ± 11	14 ± 11	38 ± 14	10 ± 30	16 ± 37	39 ± 48
DD	42	30 ± 7*	32 ± 8*	46 ± 10	55 ± 20*	57 ± 26*	67 ± 32
SD	53	79 ± 7**	72 ± 7**	93 ± 9**	155 ± 19	174 ± 23**	198 ± 29**